

## Acetyl fentanyl (*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylacetamide)

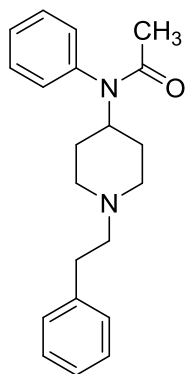
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DEA/OD/ODE

### Introduction:

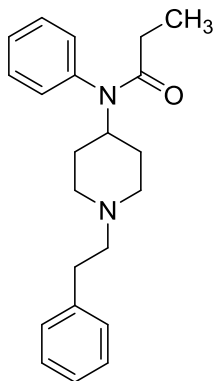
Acetyl fentanyl, similar to the Schedule II opioid fentanyl, is a potent opioid analgesic. Recently, it has been linked to a number of overdose deaths in the United States. Acetyl fentanyl is not a part of most illicit drug screens and may remain undetected in many of these cases. Immunoassays (e.g. ELISA) for fentanyl do not differentiate fentanyl and acetyl fentanyl; confirmatory analysis such as gas chromatography/mass spectrometry (GC/MS) is required to confirm the presence of acetyl fentanyl.

### Chemistry:

The chemical structure of acetyl fentanyl and the schedule II substance fentanyl are shown below.



Acetyl fentanyl



Fentanyl

Acetyl fentanyl and fentanyl are in the phenylpiperidine class of synthetic opioids. Acetyl fentanyl contains a phenylacetamide group whereas fentanyl has a phenylpropanamide group at the corresponding position. Desmethyl fentanyl is a synonymous name for acetyl fentanyl, likely due to the removal of a methylene group from the structure of fentanyl.

### Pharmacology:

Acetylfentanyl, similar to fentanyl, possesses opioid-like *in vitro* binding affinity to  $\mu$ -opioid receptors as well as  $\mu$ -opioid receptor agonist effects. Acetyl fentanyl has also been shown to inhibit the twitch response in electrically stimulated vas deferens preparation. A study using acetic acid writhing test showed that acetyl fentanyl produces analgesic response in mice and it is about 15.7-fold more potent than that of morphine. Potency of acetyl fentanyl was about 3-fold less than that of fentanyl in this assay. The ED<sub>50</sub> (the dose at which 50% of test animals had met the criterion for analgesic response) dose for acetyl

fentanyl, fentanyl and morphine were 0.021, 0.0061, and 0.33 mg/kg, respectively. Similarly, in another study using tail flick and phenylquinone writhing tests, acetyl fentanyl produced analgesic response in mice. Acetyl fentanyl has been shown to completely suppress the signs of withdrawal in morphine-dependent monkeys.

Besides analgesia, fentanyl-like substances, similar to other opioid analgesics, produce a variety of pharmacological effects including alteration in mood, euphoria, drowsiness, respiratory depression, suppression of cough reflex, constriction of pupils (miosis), and impaired gastrointestinal motility.

Clinical studies evaluating pharmacological effects of acetyl fentanyl in humans have not been reported in the scientific literature.

In acute toxicity studies in mice, the LD<sub>50</sub> (the dose causing death of 50% of test animals) of acetyl fentanyl and fentanyl are 9.3 mg/kg and 62 mg/kg, respectively. Significant bleeding in the small intestines of mice was observed in acetyl fentanyl-administered mice.

### Licit Uses:

Acetyl fentanyl has not been approved for medical use in the United States and there are no published studies on safety for human use.

### Illicit Uses:

As a  $\mu$ -opioid receptor agonist, acetyl fentanyl may serve as a direct substitute for heroin or other  $\mu$ -opioid receptor agonist substances in opioid dependent individuals. Acetyl fentanyl has been detected in tablets that mimic pharmaceutical opiate products, in powder form and spiked on blotter papers.

According to DEA's STARLiMS and National Forensic Laboratory Information System (NFLIS), federal, state and local forensic laboratories reported 10 exhibits identified as acetyl fentanyl in 2013 and 40 exhibits identified as acetyl fentanyl in 2014.

Currently, DEA is aware of at least 52 confirmed fatalities involving acetyl fentanyl in the United States in 2013-2015. Fatalities have been confirmed in California, Louisiana, Maryland, North Carolina, Oregon, Pennsylvania, Rhode Island, and Wisconsin.

### Control Status

Acetyl fentanyl is a schedule I substance under the federal Controlled Substances Act.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 202-353-1263, telephone 202-307-7183, or E-mail ODE@usdoj.gov.